Paediatric Acute Lymphoid Leukemia in Latvia in 1988–2014

Zhanna Kovalova, Sergey Nikulshin, Katrīna Latgale [1]

Children's Clinical University Hospital, Riga, Latvia
[1] *Rīga Stradiņš University, Faculty of Medicine, Latvia*

Introduction. Acute lymphoid leukemia (ALL) is the most common paediatric malignancy (30% of tumors occurring under the age of15) with excellent response to therapy; 5-year survival is about 90%. Toxicity, relapse and therapy-resistant disease are the main causes of mortality. Annual incidence in Europe is 35–60 per million children per year (mean – 46.7). There is a slight male predisposition and a sharp morbidity peak at age the 2–5.

The incidence of childhood cancer has been increasing in industrial countries; causes remain unknown, environmental and genetic factors may be responsible. Poor presentation of epidemiological data from Eastern Europe was noted in the report of the European Cancer Registry (EUROCARE-4); actually, epidemiological and clinical data on childhood ALL in Latvia have never been systematized. Efficiency of ALL-BFM treatment protocol that had been introduced in Latvia in 1992 and upgraded over the time would be of particular interest.

Aim. The aim of the study is to retrospectively analyze the incidence and survival of paediatric ALL patients in Latvia.

Material and Methods. Complete documented records for the time period of 1988–2014 are available at the Children's Clinical University Hospital Oncohematological Department (the only institution in Latvia for treatment of paediatric ALL); 341 consecutive patients entered the study, 280 were treated according to ALL-BMF program. The cohort was further subdivided by age, gender, time periods (1988–1992 – before BFM, 1993–2006 and after 2006 – treatment upgrade) and B- and T-cell variants (after 2006). Relapses were separately studied. MS Excel database was designed; statistical analysis was performed by using IBM SPSS v.21 (Kaplan-Meier for survival and Mann-Whitney U for differences).

Results. Overall annual incidence of paediatric ALL was 28.7 per million children (age 0–14). The incidence was stable in 1988–2000 (25.0 per million), but it has been increasing since 2001 (33.4 per million for the 2001–2014 period), the difference between the periods was significant ($U = 39.5$; $p = 0.011$). M:F ratio for the whole cohort was 1.26; median age was 4 years (60.6% patients 2–5 years old); 85.8% of studied cases were of B-phenotype.

10-year OS for the 280 BFM-treated patients was 0.74 and 10-year EFS 0.71 that sharply contrasted with the pre-treatment period (10-year OS 0.08, $p < 0.001$). 10-year OS in age groups 0, 1–9 and ≥ 10 was 0.25, 0.75 and 0.75, respectively, 10-year EFS 0.25, 0.73 and 0.66; the difference between infants and older groups was highly significant ($p < 0.001$ and $p = 0.002$, respectively). Survival was significantly worse in boys (10-year OS 0.67 vs 0.83, $p = 0.016$; 10-year EFS 0.64 vs 0.80) and in T-cell ALL (5-year OS 0.69 vs 0.88, $p = 0.03$; 5-year EFS 0.59 vs. 0.80). Survival increased with availability of modern diagnostics and stem cell transplantation (hSCT), 1993–2006 vs. 2007–2014: 5-year OS 0.74 and 0.85, 5-year EFS 0.70 and 0.77, respectively; difference non-significant. Relapses were the main cause of death, 5-year OS in relapsed patients was only 0.26 vs. 0.93 in non-relapsed cases, $p < 0.001$. Relapse rate in the whole cohort was 21.4% and stable: 21.8% in 1993–2006 and 20.7% in 2007–2014. Average time to relapse was 2 years, 17 patients (28.3%) relapsed after 3 years and later. Relapse survival significantly improved after 2006: 3-year OS increased from 0.10 to 0.26 ($p = 0.01$).

Conclusions. The incidence of paediatric ALL in Latvia is noticeably lower than reported in Europe, but it is steadily growing, which may be a part of the international trend. Gender, age and phenotypic distributions are unremarkable. Access to the contemporary BFM-based therapy during the independence time has dramatically improved the patients' survival that has increased 10-fold. Additional diagnostic options and hSCT since 2006 further improved the outcome, particularly in relapsed patients. Incidence dynamics and the relatively high proportion of late relapses may suggest a possibility of a tumor-predisposing factor existing in population.